

REMARKS

Claims 8, 14, 16 and 18 are pending in this application. Claim 8 is amended herein. Claims 1-7 and 9-13, 15 and 17 were previously cancelled. Support for the amendment of claim 8 may be found, for example, as follows. Isolation of the fusion protein is described in Example 2, p. 13-14, of the application as filed. Obtaining a binding complex extracellularly is described in Example 3, p. 14-15, of the application as filed. Delivery of the fusion protein into a cell *in vitro* is described in Example 4, p. 15, and delivery of the fusion protein into a cell *in vivo* is described in Example 5, p. 15-16, of the application as filed. Thus, the claim amendments are believed to be fully supported in the original application.

Applicants respectfully request entry of the present after-final Reply for the following reasons. This Reply only adds claim limitations, the absence of which was contended in the Office Action to make the evidence and arguments not commensurate with the scope of the claims. Applicants respectfully submit that the present after-final amendment should be entered, since the presently submitted amendments both render the claims allowable and do not raise new issues not previously considered by the Office.

Regarding the statement in the Office Action that "nothing in the claims indicates that the binding complex was obtained outside the cell and then delivered into the cell", Applicants respectfully submit that the presently submitted claims directly address this point and therefore Applicants' previously submitted arguments should be reconsidered.

Regarding the statement in the Office Action that "in fact, claim 16 has the delivery of the binding complex occurring *in vivo* or *in vitro*", Applicants respectfully note that, the claims explicitly recite in step v) "Delivering the binding complex of step iv) into cytoplasm or nucleus". This means that the binding complex is delivered into a cell. This does not mean that the cell cannot be either *in vivo* (i.e., in a living being) or *in vitro* (i.e., in a test tube), which is what claim 16 recites, it only means that the binding complex, which has been obtained extracellularly in the step iv) is thereafter delivered to an intracellular location, i.e., into cytoplasm or nucleus.

There is nothing inconsistent in these claim recitations or between these claim recitations and the evidence.

Thus, Applicants respectfully submit that the scope of the claims is commensurate with the scope of both the disclosure, the evidence and the previously submitted arguments.

Rejections of Claims over Ye et al. in view of Zuckerman

Claims 7-9 and 14 stand rejected as obvious over Ye et al. in view of Zuckerman. Applicants respectfully traverse this rejection for at least the following reasons.

Applicants incorporate by reference the previously submitted arguments and evidence. In addition, Applicants respectfully submit the following additional points.

The Office Action stated “Ye et al produce expression vectors of chimeric proteins incorporating the transcriptional activator and PTD, and tests the ability of the PTD to deliver the protein in a cell by luciferase activity in a cell which is already transfected with the Gal4-luciferase reporter vector, as opposed to the present invention wherein the binding complex was obtained outside the cell, and then delivered into the cell.” Thus, according to the Office Action, the difference is between the binding complex being formed inside the cell from separately delivered components (Ye et al.) and the binding complex formed outside the cell and then delivered into the cell (present invention).

Applicants have amended the claims to specifically recite that the fusion protein is isolated, that this is combined with the recombinant expression vector to thereby obtain the binding complex extracellularly.

The Office Action states that the Applicants' arguments have not been found persuasive because “Nothing in the claims indicates that the binding complex was obtained outside the cell and then delivered into the cell. In fact claim 16 has the delivery of the binding complex occurring *in vivo* or *in vitro*.” Based on and in response to this statement, Applicants have amended the claims to specify that the binding complex is obtained outside the cell and delivered into the cell. This strengthens the distinction over Ye et al. and, Applicants respectfully submit,

overcomes the rejections.

In this regard, Applicants note that the claims state, in step (v), that the binding complex, formed in step (iv), is delivered into cytoplasm or nucleus. To the extent that the claims were considered to read on embodiments in which the binding complex would be formed inside the cytoplasm or nucleus, the claim amendments fully distinguish such reading.

As noted above, Applicants consider that, contrary to the assertions above with respect to claim 16, it should not matter if the target cell is located *in vivo* or *in vitro* at the time the binding complex is delivered into the cell. The point is that the extracellularly-formed binding complex is delivered into the nucleus or cytoplasm of a cell, as specified in claim 8. Thus, there is no contradiction or inconsistency between claim 16 and claim 8. The fact that the target cell may be in a living being or in a test tube is not the point; the point is that the binding complex is formed extracellularly and is thereafter delivered into a cell.

Accordingly Applicants respectfully submit that the foregoing claim amendments, previously submitted evidence and the arguments herein and previously submitted clearly demonstrate that the presently claimed invention of claims 8, 14, 16 and 18 would not have been obvious. Therefore, Applicants respectfully request withdrawal of the asserted rejections and allowance of the claims. Notice to such effect is respectfully requested.

Conclusion

For the reasons set forth in the foregoing, Applicants respectfully submit that the present application is in condition for allowance, and an early notice to such effect is respectfully requested. For the same reasons, Applicants respectfully request entry of the present after-final Reply, since it is believed that it renders the claims into condition for allowance.

Should the Examiner consider that a telephone interview would be helpful to facilitate favorable prosecution of the above-identified application, the Examiner is invited to contact the undersigned at the telephone number provided below.

Petition and the fee for a three-month extension and for an RCE is submitted herewith. The assignee of the present application is a small entity, and the fees submitted are for a small entity. If any additional fees are required for the filing of this paper, Applicants request the Commissioner to charge the fees to deposit account #18-0988, Dkt. No. NAMNP0103US.

Respectfully submitted,

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